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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,957	07/21/2004	Samuel G. Steinemann	S0004/7003US0	8443

21127 7590 02/02/2010

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EXAMINER
HEYER, DENNIS

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
02/02/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/501,957	STEINEMANN ET AL.	
	Examiner	Art Unit	
	DENNIS HEYER	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of Applicant's remarks and amendments filed April 16, 2009. Acknowledgement is made of Applicant's amendment to Claims 28, 30, 40, 42 – 47 and 51 and the addition of new Claims 52 – 70 in the response filed September 23, 2008. Acknowledgement is also made of Applicant's submission, received August 4, 2009, of a paper and a computer readable copy of the disclosed amino acid sequences and a statement of support which places said submission in accordance with 37 C.F.R. §§ 1.821 – 1.825. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 28 – 70 are currently pending.

Priority

This application, 10/501,957, filed July 21, 2004 is a national stage entry of PCT/CH03/00013 , International Filing Date: January 14, 2003. This application claims foreign priority under U.S.C. § 119 of Swiss patent application CH88/02, filed January 21, 2002.

Withdrawn Rejections

Claim rejections – 35 USC § 103

The rejection of Claims 28 – 34 and 42 – 51, as being unpatentable under 35 U.S.C. 103(a) by Copf in DE 19949890 is withdrawn in response to Applicant's arguments.

The rejection of Claims 35 – 41, as being unpatentable under 35 U.S.C. 103(a) by Copf in DE 19949890 in view of Atkinson *et al.* in US patent 6,511958, is withdrawn in response to Applicant's arguments.

New Rejections

Applicant's arguments filed September 23, 2008 with respect to the withdrawn rejections cited above under 35 U.S.C 103(a) are found to be persuasive. Accordingly, in view of the Applicant's arguments, amendments and the addition of new Claims 52 – 70 , a new ground of rejection is presented below.

Claim rejections – 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28, 41, 51, 52 and 70 are rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28, 51, 52 and 70 recite the phrase "surface covered with a polypeptide *at a rate of* 5 to 70% (or 8 to 20%) based on a maximum coverage of the metal surface with a monomolecular layer". The term "at a rate of" is unclear. Applicant's intention may have been to state "having 5 to 70% of the surface of the metal covered with a monomolecular layer of polypeptide". The latter represents the *extent* of the surface upon which the polypeptide is coated. The claim, as currently worded, reflects a *rate* which would typically include a time variable (such as micrograms per minute) over which the desired coverage would be achieved.

Herein and for the purposes of examination on the merits, with respect to the prior art said "rate" limitations are considered by the Examiner as meaning 'the percent of the surface coated by the polypeptide' or 'at a rate of' as currently recited in the instant Claims. The interpretation of the claim limitation drawn to a "rate" as meaning the "percent surface coated" with the polypeptide is supported by Example 1 of the instant specification.

Claim 51 also recites the term "wherein the metal surface is covered with the polypeptide" with respect to an osteogenic dental implant. There is insufficient antecedent basis for this limitation in the claim. The term "metal surface' has not been

defined. Claim 51 also recites the term "wherein the bone surface, in the area of the cavity" with respect to the cavity of a jaw bone. There is insufficient antecedent basis for this limitation in the claim. The term “bone surface” has not been defined.

Further, Claim 51 appears to recite a process for introducing an osteogenic dental implant but, since the claim does not set forth any active steps (For example ‘A process….comprising the steps of…) involved in the method/process, it is unclear what method/process applicant is intending to encompass. Applicant is required to provide a clarification of these matters or correlation with art-accepted terminology so that a proper comparison with the prior art can be made. Applicant should be careful not to introduce any new matter into the disclosure (i.e., matter which is not supported by the disclosure as originally filed). For the purpose of examination on the merits, limitations drawn to a process of introducing (inserting, placing or administering) a dental implant as disclosed in the prior art will be considered as reading on ‘bringing the implant in contact with the bone surface.’

Claim 41 recites the limitation "the implant of Claim 28, wherein the systemic hormone comprises one or more of 1, 25-$(OH)_2D_3$, 1α, 1-$(OH)_2D_3$ and 24, 25-$(OH)_2D_3$" There is insufficient antecedent basis for this limitation in the claim. Instant Claim 28, from which Claim 41 depends, requires that the systemic hormone be a polypeptide. The systemic hormones cited in instant Claim 41 are, in fact, non-peptide steroid-based vitamin D compounds. In view of the lack of clarity of the term systemic hormones (polypeptide and/or steroid hormone), for the purpose of examination on the merits,

limitations drawn to solution concentrations and percent surface coated as disclosed in the prior art will be considered as reading on both polypeptides *and* systemic hormones.

Claim rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28, 31, 33, 44, 48, 51, 52 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Cole *et al.* in Clinical Orthopaedics and Related Research, 345, 219 – 228 (1997) as evidenced by Schrier *et al.* in AAPS PharmSciTech 2001; 2(3) article 18 and Israel *et al.* in US 2008/0139474 (published June 12, 2008).

Cole *et al.* teach that the transforming growth factor, human bone morphogenic protein (BMP-2), enhances bone formation in rats by direct application to a titanium implant surface (Abstract, page 227, final paragraph; instant Claims 28, 31, 33). BMP-2 contains the amino acid tryptophan which has a heterocyclic ring (instant Claims 40 and 56) as evidence by Israel *et al.* (Figure 1, amino acid sequence of BMP-2). Cole teaches bringing a roughened cylindrical titanium implant into contact with a BMP-2 stock solution of 2300 µg/mL (~ 78 µmol/L) (page 220, Recombinant Human Bone Morphogenic Protein Section) which is within the limitation of polypeptide concentrations recited in instant Claims 44 and 48. Note that the molar concentration

of BMP-2 was calculated using a molecular weight of 32K Daltons as evidenced by Schrier *et al.* ("rhBMP-2 is a 32-kd homodimeric protein"; page 1, Introduction, 3rd paragraph).

Accordingly, although Cole does not explicitly teach the "rate" or, the percent of the titanium surface, coated with monomolecular layer of polypeptide, because Cole teaches bringing the same polypeptide (BMP-2) solution into contact with a roughened titanium implant at the same concentrations recited in instant Claims 44 and 48, the amount of the surface of the titanium implant coated will fall into the same ranges recited in instant Claims 28, 51, 52 and 70. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." In the instant case the Applicant merely *characterizes* the percent surface coated by the polypeptide BMP-2 in the titanium implant of Cole (Claims 28, 51, 52 and 70). Accordingly, absent a specific showing of evidence to the contrary, the composition of Cole has the same percent surface coated with a monomolecular layer of polypeptide.

Claim rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28 – 31, 33, 40, 42 – 60 and 63 – 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinemann *et al.* in WO00/44305; published: August 03, 2000, in view of Cole *et al.* in Clinical Orthopaedics and Related Research, 345, 219 – 228 (1997) as evidenced by Schrier *et al.* in AAPS PharmSciTech 2001; 2(3) article 18 and Israel et al. in US 2008/0139474 (published June 12, 2008).

It is noted that, for ease of examination, the Examiner relied upon US Patent 6,702,855 as an equivalent English translation of the German language application

PCT/EP00/00619 (WO 2000/44305). US Patent 6,702,855 is a national stage entry of PCT/EP00/00619 (WO 2000/44305). All citations henceforth to Steinemann *et al.* are located in the US Patent.

Steinemann teaches an osteophilic implant with improved osteointegration properties. The implant is made of titanium metal whose surface is partially roughened and in the hydroxylated state (Abstract; instant Claims 28 and 29). The macro- and micro-roughness limitations on the titanium surface of the implant are taught by Steinemann on column 3, lines 52 – 59 and in Example 1 (column 7, lines 26 – 35; instant Claims 30 and 53 – 55).

Regarding packaging of the implant, Steinemann teaches the implant is packaged "preferably sealed in a gas-tight and liquid-tight covering" (column 5, lines 30 – 38) and that the implant assembly comprises a vessel having an inert atmosphere and a medium that is at least partially filled with water (column 5, lines 43 – 46, Claims 2 and 4 – 6; instant Claims 42 and 57 – 58). The limitation of packaging the implant in "pure water' is taught in Example 1, lines 40 – 41.

Steinemann teaches that suitable additives are incorporated into pure water including mono- and divalent cations and anions in amounts ranging from 50 to 250 meq/l (column 5, lines 57 – 67 and column 6, lines 1 – 14; instant Claims 45 – 46, 59 and 63 – 66).

Steinemann teaches a process for roughening the implant surface by initial sandblasting and a subsequent chemical etching process (column 7, Example 1, lines 26 – 35, Claims 37 – 39; instant Claims 67 – 69), with the resulting material being an

implant, as well as a dental implant (column 7, lines 47 – 51, instant Claims 47 and 49 50). Further, Steinemann teaches a process for introducing a partially cylindrically shaped dental implant into the cavity of a jaw bone (column 7, lines 47 – 52, instant Claim 51).

Steinemann does not teach an osteogenic implant comprising polypeptides.

Cole *et al.* teach that the transforming growth factor, human bone morphogenic protein (BMP-2), enhances bone formation in rats by direct application to a titanium implant surface (Abstract, page 227, final paragraph; instant Claims 28 – 29, 31, 33, 47 and 51). BMP-2 contains the amino acid tryptophan which has a heterocyclic ring (instant Claims 40 and 56) as evidence by Israel *et al.* (Figure 1, amino acid sequence of BMP-2). Cole teaches bringing a roughened cylindrical titanium implant into contact with a BMP-2 stock solution of 2300 µg/mL (~ 78 µmol/L) (page 220, Recombinant Human Bone Morphogenic Protein Section) which is within the limitation of polypeptide concentrations recited in instant Claims 44 and 48. Note that the molar concentration of BMP-2 was calculated using a molecular weight of 32K Daltons as evidenced by Schrier *et al.* ("rhBMP-2 is a 32-kd homodimeric protein"; page 1, Introduction, 3rd paragraph).

Accordingly, although Cole does not explicitly teach the "rate" or, the percent of the titanium surface, coated with a monomolecular layer of polypeptide, because Cole teaches bringing the same polypeptide (BMP-2) solution into contact with a roughened titanium implant at the same concentrations recited in instant Claims 44 and 48, the amount of the surface of the titanium implant coated will fall into the same ranges

recited in instant Claims 28, 51, 52 and 70. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In In re Crish, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." In the instant case the Applicant merely *characterizes* the percent surface coated by the polypeptide BMP-2 in the titanium implant of Cole (Claims 28, 51, 52 and 70). Accordingly, absent a specific showing of evidence to the contrary, the composition of Cole has the same percent surface coated with a monomolecular layer of the polypeptide.

It would have been *prima facie* obvious for one of ordinary skill in the art to cover the titanium surface of Steinemann with a bone morphogenic protein, such as BMP-2 to provide an osteogenic implant. One would have been motivated to do so, at the recited concentration ranges, with a reasonable expectation of success, because Cole teaches that the combination of BMP-2 on a roughened titanium implant surface is osteogenic, i.e. enhances bone formation, in rats.

Claims 41 and 61 – 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinemann *et al.* in WO00/44305; published: August 03, 2000, in view of Cole *et al.* in Clinical Orthopaedics and Related Research, 345, 219 – 228 (1997) as evidenced by Schrier *et al.* in AAPS PharmSciTech 2001; 2(3) article 18 and Israel et al. in US 2008/0139474 (published June 12, 2008), as applied to Claims 28 – 31, 33, 40, 42 – 60 and 63 – 70, and further in view of Lohmann *et al.* in Journal of Bone and Mineral Research, 15, 1169 – 1180 (2000).

Steinemann in combination with Cole teach an osteogenic implant, and preparation thereof, of a micro and macro roughened titanium surface and a polypeptide within the recited concentration and percent coating limitations.

The combination of Steinemann and Cole do not teach the systemic hormones as recited in instant Claim 41 nor the limitations of contacting the titanium metal surface with a peptide or systemic hormone solution a the lower ranges from 0.1 to 10 µmol/l or about 1 µmol/l (instant Claims 61 and 62). As noted above, Claim 41 has been rejected for lacking antecedent basis because the compounds recited are not peptides.

Lohmann teaches the response of osteogenic cells to surface roughness and 1,25-dihydroxyvitamin D_3 (1,25-$(OH)_2D_3$ (Title). Lohmann teaches osteogenic cell differentiation was enhanced on roughened titanium surfaces, and further enhanced by the addition of 1,25-$(OH)_2D_3$ at a concentration of 10^{-7} M (0.1 µmol/l; Abstract, instant Claims 40 and 61). This concentration is within the range recited in instant Claim 61.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to contact the titanium implant at the lower

polypeptide or hormone concentrations taught by Lohmann as this is an art-recognized concentration shown to produce an osteogenic effect on a roughened titanium surface. Moreover, generally, differences in ratios of excipients in a formulation will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such ratios are critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Regarding the limitation of 1 µmol/l recited in instant Claim 61, this concentration falls between the higher (Cole) and lower (Lohmann) concentrations taught in the prior art. Accordingly, it would have been prima facie obvious to use an intermediate concentration as Applicants have not demonstrated any unexpected or unusual results, which accrue from a concentration of 1 µmol/l.

Claims 34 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinemann *et al.* in WO00/44305; published: August 03, 2000, in view of Cole *et al.* in Clinical Orthopaedics and Related Research, 345, 219 – 228 (1997) as evidenced by Schrier *et al.* in AAPS PharmSciTech 2001; 2(3) article 18 and Israel et al. in US 2008/0139474 (published June 12, 2008), as applied to Claims 28 – 31, 33, 40, 42 – 60 and 63 – 70 above, and further in view of Brager *et al.* in Journal of Orthopaedic Research, 18, 133 – 139 (2000) as evidenced by Bab *et al.* in EMBO 11, 1867 – 1873 (1992).

Steinemann in combination with Cole teach an osteogenic implant, and preparation thereof, of a micro and macro roughened titanium surface and the

transforming growth factor polypeptide (BMP-2) within the recited concentration and percent coating limitations.

The combination of Steinemann and Cole do not teach the limitation of instant Claims 34 and 39, in which the transforming growth factor polypeptide is osteogenic growth peptide.

Brager *et al.* teach the effect of administering exogenous osteogenic growth factor on fracture healing in the rat (page 138, discussion) as evidenced by increased mitogenicity and osteogenicity of marrow colonies in treated animals relative to controls (page 139, 2nd paragraph). The Brager reference, as noted above, teaches the osteogenic effect of the 14 amino acid polypeptide OGP (page 133, summary, 1st sentence) but does not disclose the sequence. As evidenced by, Bab *et al.*, the aforementioned 14 amino acid polypeptide is identical in sequence to that recited in instant Claim 39 (Bab, page 1868, Table 1).

It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to cover the titanium implant of Steinemann with the known osteogenic polypeptide OGP. One would have been motivated to do so, with a reasonable expectation of success of providing an osteogenic implant, because administered OGP is known (Brager) to increase osteogenicity in fractures in the rat and other known transforming growth factor polypeptides such as bone morphogenic protein (BMP-2) when applied to a titanium implant (Cole) also provide an osteogenic effect.

Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Steinemann *et al.* in WO00/44305; published: August 03, 2000, Cole *et al.* in

Clinical Orthopaedics and Related Research, 345, 219 – 228 (1997), as applied to Claims 28 – 31, 33, 40, 42 – 60 and 63 – 70 above, and further in view of Schmidmaier *et al.* in Bone, 28, 341 – 350 (2001).

Steinemann in combination with Cole teach an osteogenic implant, and preparation thereof, of a micro and macro roughened titanium surface and the transforming growth factor polypeptide (BMP-2) within the recited concentration and percent coating limitations.

The combination of Steinemann and Cole do not teach the limitation of instant Claim 32, in which the transforming growth factor polypeptide is selected from the transforming growth factors beta (TGF-β).

Schmidmaier *et al.* teach that local application of growth factors such as TGF-β1 on osteosynthetic implants accelerated fracture healing in rats (Title). Schmidaier teaches that locally applied TGF-β1 accelerates fracture healing in a dose-dependent manner (page 341, Introduction, 2nd paragraph). Schmidaier further teaches the effect on fracture healing in the rat with a titanium implant comprising TGF-β1 (page 343, Figure 1).

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time of the invention, to cover the titanium surface of Steinemann with a transforming growth factor such as TGF-β1. One would have been motivated to do so with a reasonable expectation of successfully providing an osteogenic implant because Schmidmaier teaches an accelerated healing effect on a bone fracture (an osteogenic effect) with a titanium implant coated with TGF-β1.

Claims 34 – 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinemann *et al.* in WO00/44305; published: August 03, 2000, Cole *et al*. in Clinical Orthopaedics and Related Research, 345, 219 – 228 (1997) as applied to Claims 28 – 31, 33, 40, 42 – 60 and 63 – 70 above, and further in view of Kale *et al.* in US patent 6,811,776, filed: December 27, 2000 as evidenced by Bergmann in US patent 5,168,041).

Steinemann in combination with Cole teach an osteogenic implant, and preparation thereof, of a micro and macro roughened titanium surface and the transforming growth factor polypeptide (BMP-2) within the recited concentration and percent coating limitations.

The combination of Steinemann and Cole do not teach the limitation wherein the polypeptide is osteocalcin (instant Claim 34) or an osteocalcin having the formulas recited in instant Claims 35 – 38. It is noted that because the claims employ 'open language' the limitations are reasonably interpreted broadly as an osteocalcin comprising the recited sequences.

Kale teaches a method for *ex vivo* bone formation in the presence of osteogenic growth factors in addition to cDNA's encoding extracellular matrix proteins such as osteocalcin (column 4, lines 3 – 10). Kale further teaches that osteocalcin occupies 20% of the non-collagen protein of the bones and is presumed to have an important role in the formation of bone matrices (column 10, lines 66 – 67 and column 11, lines 1 – 9).

Kale teaches that human osteocalcin is a 49 amino acid protein but does not disclose the amino acid sequences for the osteocalcins recited in Claims 35 – 39. The

sequences recited in Claims 35 – 39, as evidenced by Bergman, correspond to those found in human osteocalcin (Bergman, column 1, lines 24 – 30).

It would have been *prima facie* obvious to coat the titanium implant of Steinemann with the osteocalcin sequences corresponding to human osteocalcin. One would have been motivated to do so because Kale teaches that osteocalcin is a major component of protein in bones and has an important role in forming bone. Further, it would have been *prima facie* obvious to use amino acid sequences comprising human osteocalcin as a coating on the titanium implant of Steinemann with a reasonable expectation that the resulting composition would play a role in bone formation.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg,* 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman,* 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel,* 422 F.2d 438,

164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28 – 31, 33, 40 – 60 and 63 – 70 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1 – 41 of Steinemann *et al.* in **US patent 6,702,855** in view of Cole *et al.* in Clinical Orthopaedics and Related Research, 345, 219 – 228 (1997).

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons below:

The instant and copending Claims (Steinemann) are both drawn to surface modified (roughened) osteogenic titanium implants. Steinemann claims an implant comprising titanium having a roughened surface which is hydroxylated,, Steinemann claims an implant assembly comprising the titanium implant and a vessel at least partially filled with water and inorganic salt additives. Steinemann claims a process for roughening the titanium surface by electrochemical or chemical etching. Steinemann

does not claim covering the surface of the implant with a polypeptide. Cole teaches covering a titanium implant with the polypeptide BMP-2 and teaches said polypeptide-covered implants are osteogenic, i.e. enhance bone formation in rats.

It would have been *prima facie* obvious for one of ordinary skill in the art to cover the claimed titanium surface of Steinemann with the bone morphogenic protein, BMP-2, taught by Cole, to provide an osteogenic implant. One would have been motivated to do so, with a reasonable expectation of success, because Cole teaches that the combination of BMP-2 on a roughened titanium implant surface is osteogenic, i.e. enhances bone formation, in rats.

Conclusion

Claims 28 – 70 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DENNIS HEYER whose telephone number is (571)270-7677. The examiner can normally be reached on Monday-Thursday 8AM-5PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, BRANDON FETTEROLF can be reached at (571)272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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DH

/Brandon J Fetterolf/

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